THE

HISTOCHEMISTRY

AND

PATHOGENY OF TUBERCLE

BY

WILLIAM THOMSON F.R.C.S. EDIN.

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"A subject as yet but little studied in English-speaking "countries."

"And I cannot but think that a greater effort should be "made by all medical men who love progress, to vindicate "the dignity of Pathological Histology as a science in "this country, and to raise it above the complacent "smiles of a large class appropriating to themselves the "title of 'the thoroughly practical,' who, for the most "part, ignorant of its most elementary principles, appear "to regard it as merely the pet hobby of a few vague "theorisers and entirely unprofitable."—A. E. Barker.

"This minute discussion is of importance in reference "to our general comprehension of tuberculosis."

Rindfleisch.

"But even an hypothesis may be of advantage to the "facts by bringing valuable criticism to bear upon them, "and by showing not only how to formulate the questions, "but also in which direction to push inquiries, in order "that it may be possible to reach an accurate decision "as to what is the truth."—Liebermeister.

PREFACE

This essay is the expansion of the pathological argument alluded to at page 38 of the *Third Analysis, &c., of Phthisis.* It was intended for a third section of that paper, but from its technical form it is now printed apart.

After the whole was in type I had an opportunity of reading the debate on syphilis at the Pathological Society of London, and could now corroborate my view by reference to the remarks of several speakers; but rather than alter I prefer to leave the observations as they at first occurred to my own reflection. The similarity of idea between that and many of the thoughts then expressed is evident; and although the taking apothegm of a "flesh and blood disease," told effectively upon the audience, scientific doubts will in the end be better resolved by the more definite theory.

On the other hand, to speak of "a certain potentiality" as the cause, is, with profound deference be it observed, mere philosophical negation, safe rather than suggestive; for every potential has its material form. Finally, from the still later discovery of like organic bodies as essentially causative elements in the histology of leprosy, there is derived another collateral probability that the new theory is true.

HISTOCHEMISTRY & PATHOGENY OF TUBERCLE.

"An element of which modern anatomy alone has "conceived the importance—epithelium."—Küss.

It is admitted by the best authorities that medical science has not yet found a theory of tuberculosis.* Histology and histochemistry bring the problem near solution, but leave room for conjecture. Therefore, although a pioneer in such inquiries enjoins caution in using "the liberty to guess,"† a carefully stated essay may prove useful; and cannot do harm if the unproven hypothesis lead to no fanciful scheme of treatment. The following

* "Pathologists are much exercised in mind as to what "is tubercle and what is phthisis."—*Practitioner*, April "1875. "Altogether, the question is one of extreme "difficulty, and cannot be said to be as yet set at rest."—*Pathological Anatomy*. Jones and Sieveking, by Payne, 1875.

† Sir James Paget, *Clinical Essays*, 1875.

remarks, here thrown into the form of interrogative suggestion, may have no more merit than in agreeing with long known facts and later discoveries in this department of special pathology. "To argue too far from incomplete "data would, seeing the history of biological "chemistry during the last thirty years, be a "deplorable error."* Since it is yet the case that in health, "the activities of the body, "which result from chemical changes, depend "upon conditions with which we are unac-"quainted,"† only the most guarded inferences can be safely drawn from that limited knowledge in endeavouring to describe any process of disease.‡ At present there exists only a

* Dr. Thudichum, *Priv. Coun. Rep.*, 1874.

† Professor Hermann, *Human Physiology*, 1875.

‡ Even Dr. Dobell, in enouncing his purely chemical etiology of tubercle, admits the great difficulty to be in the "many important points in physiology unavoidably involved "in every theory of nutrition, whether normal or abnormal, "in which our knowledge is, at best, vague or unsatisfac-"tory," and hence his invocation of the aid of those having "profound physiological and chemical knowledge." His hypothesis—that the want of alkaline pancreatic fluid to emulsify fat, leads to the abstraction of fatty elements from the albuminoid tissues, the residual elements of which,

rudimentary histochemistry. "Without a know-
"ledge of composition, true scientific study of
"histology is impossible, and the latter is in
"danger of degenerating into mere toying with
"details of form."* When pathologists speak of the softening of homogeneous tubercle as resulting from simple chemical changes, little is said of their nature, although it is evident that until that be known clinical work with them must be empirical.

Tubercle, in the natural disease of the human body, in contra-distinction to an artificially-induced disease of animals experimented upon,†

being thus disintegrated, form tubercle—was defective in not explaining the histology of the morbid product. It is curious that while a recent pathology of tuberculisation should have its inception in the inactive pancreas, Louis, in his great *Organon*, never noted the condition of the gland, although Dr. Austin Flint, in his *Clinical Study of Phthisis*, states that "Louis examined all the viscera."

* Prof. Frey, *Histochemistry*, 1874.

† Among chemico-histologists, Friedländer and Orth have lately taken opposite views upon this point of identity or difference, but the account referred to in the text appeared to me to be conclusive; and Ruehle thinks so, likewise, for he remarks that "there is no evidence whatever that the artificially induced disease in inoculated animals is identical with human tuberculosis."

forms, according to the latest researches of Dr. Klein, in the epithelium on the walls of the alveoli of the air vesicles, the ultimate and true respiratory membrane.* The very existence of this epithelium was long disputed, and the doubt formed a bar to any explanation akin to the one now offered. The constant and necessary presence of this epithelium has, however, been fully demonstrated.† This epithelial layer is formed from an exudation of protoplasm from the capillaries of the bronchial arteries, the proper nutrient blood-vessels of the lungs, the capillary vessels of the pulmonary artery being alone for the respiratory function, and not nutritive of the lung parenchyma.‡ The transudation of protoplasm

* That is, leaving out of present view the respiratory action going on in the tissues of the body. The air vesicles and alveoli are often alluded to as being synonymous; but in discussing their intimate anatomy the alveoli and alveolar sacs should be distinguished as different parts of an acinus of the lung. The floor of every sac or proper aërating chamber is covered with pits or *alveoli*.

† See Küss and Duval, *Man. of Phys.*, p. 192, 1875.

‡ According to Schulze, the two sets of capillaries mingle their currents by free anastomoses, and Chauveau offers the same view as the one held by competent authorities;

is in healthy action continuous, forming new epithelial cells as the old ones are shed off on finishing their special work. This statement may appear too absolute; since some histologists think there is no renewal of epithelium, but only a shrinking of the protoplasm with the progress of formed material of the epithelial scale on the alveolar wall. But, judging by analogy of all epithelial growths and renewals, as well as from the pathological deposits of dead epithelium in the air chambers: from its rapid and abundant proliferation in acute catarrhal pneumonia, for instance, the normal process of growing epithelium in the air vesicles is most probably that as described.* It is affirmed by Rindfleisch, who also adds Buhl's opinion to the same effect, that the air chamber epithelium resembles the endothelium of serous membranes rather than that of the

but Frey, citing Henle, gives what appears to be the true account of the flowing of the blood from the capillaries of the bronchial arteries, ramifying on the walls of the alveoli, into the pulmonary veins. See Stricker, *Hist.*, p. 443, and Frey, *Hist.*, p. 454; or Chauveau, *Comp. Anat.*, p. 470.

* "The pulmonary epithelium is quickly regenerated."—Prof. Juergensen, *Prof. Von Ziemssen's Cyc.*, vol. v. p. 48.

mucous membrane of secreting glands; but both authors describe an abundant reproduction of its cells in desquamative or catarrhal pneumonia.* In the croupous form of pneumonia the increase of epithelium is quickly removed by its solution and absorption; but the debris of epithelium forming tubercle can neither be absorbed nor escape through the narrow infundibulum of the air vesicle. This would furnish an anatomical basis for the epithelial theory of tubercle and phthisis, and obviate the necessity of following the suggestion of Dr. Moxon, to make the classification of the varieties of phthisis clinical rather than pathological. A clinical classification is one of mere convenience for carrying on what is at best but a tentative method of treatment; but a strictly causative classification can alone bring the preventive or curative management of the tubercular fever, or its correlated pathological sequel, phthisis, up to the level of scientific precision: that is, if it be directed according to the nature of the

* *Ziemssen's Cyc.*, vol. v. p. 665, 1875.

proximate cause. If, for instance, that cause be a parasitic organism, the treatment must vary from that suitable for ordinary scrofulous inflammation, with which the tubercular process is held by very many pathologists to be identical. The same special exciting cause of tubercle might give the key to the full distinction between all forms of true phthisis and alveolar catarrh, or indeed of every form of bronchitis or pneumonia, which even the elaborate differentiations of modern writers have scarcely yet supplied.* Thus, Professor Juergensen admits that "until recently croupous pneumonia belonged to those diseases which were supposed to be accurately understood, and yet more thorough study has gradually revealed the imperfection of our knowledge." †

When, under the morbid influence of the cause of tubercular disease, the histological nature of which will be presently referred to, two or more epithelial cells, with their nuclei, fuse together, they form the giant cell des-

* See *Natural History and Relations of Pneumonia*, by Octavius Sturges, M.D., &c., p. 180, 1876.

† *Ziemssen's Cyc.*, vol. v. p. 5.

cribed by Schüppel, now known to be peculiar to tubercle,* a giant cell being only a mass of the *débris* of epithelial cells matted together on the alveolar wall. Lying imbedded in this mass are vast numbers of minute granular bodies of faintly-defined homogeneous structure, the exact nature of which is not yet finally made out. Alluding to them, Dr. Klein remarked that by Professor Klebs they might be considered true micrococci. So defined, these living protozoic organisms of specific type, are analogous to, if not identical with, the microzymes or protomycetes which are thought, by very many leading pathologists, to be the really active particles in at least several distinct forms of specific contagia. Very similar particles have been disclosed by the minute anatomy of leprosy, in the form of whitish granules lying in the stroma formed by the material of infiltration, and in the

* In the last *Gulstonian Lecture*, 1876, Dr. Shepherd gave it as his belief that the giant cell theory would be relegated to oblivion, because the cells are only epithelial; but for that very reason, I think the theory will abide to reveal the great secret.

brownish granules enclosed in the nuclei remaining in the vacuole of the cell-wall, after it has been drained (by the parasite?) of its living protoplasm.* Although Dr. Klein does not admit that those minute particles are micrococci, neither has he as yet wholly denied the probability of their being such, merely doubting whether the tests for micrococci suffice to identify them in proof of their specific organic character. The bodies are, however, invariably found among the giant cells; there can be no doubt about their presence, because they have always been seen by every one who has looked for them; it is only the significance of their being that is not yet seen by the mental eye; and, if they be not microzymes, their precise nature still remains unknown. They appear to be identical with the "faint homogeneous bodies" that are thought by Schüppel to originate *de novo* in protoplasts, forming the nuclei of the giant cells.† Dr. Bastian would probably believe,

* Prof. Aitken, *Sci. of Med.*, i. 936, 6th ed. 1872.

† At least seven elements are required to form a living organism, viz., C. H. O. N. P. K. Ca. Several others are

with Schwann and Empis, that bodies of the kind might arise by heterogenesis in enfeebled protoplasm, and form the granulia, or particles otherwise known by those who, with Dr. Wilson

also essentially present in particular organisms, as Fe., Si., Mn., S., Na., Mg. Of those enumerated, the first five are stable elements in the albuminoid molecule; and invariably exist, even in the lowest organisms; but the other two, earth metals, may be replaced by other mineral elements of the same category.

No substance known to science contains all those elements as its constituents, except such as had, at one time, formed a proximate principle of a living organism.

No living organism was ever known, that did not contain all those elements coexisting in some one or more of its albuminoid or proximate principles.

Never have the phenomena of living matter, or life, been manifested, where those seven elements did not coexist, or perhaps, even chemically combine.

By no direction of kinetic force have those elements been synthetically combined into the constituents of any one homogeneous substance, or endued with potential energy, except under the direct influence of a living organism, and, for the most part, immediately out of matter, containing them, that formerly lived.

If any one of those essential elements be removed, or withdrawn from living matter, the remainder are instantly reduced to the inanimate state.

Therefore, since no dynamic power, uncorrelated to living forms, can cause those seven essential elements to mingle, or combine, it is impossible to predicate the evolution of life out of matter, except by a determining living organism; and, hence, the axiom *omne vivum e vivo* must be true.

Fox, still adhere to the specific pathology of Bayle and Laennec, as the grey granulations of tuberculosis. Perhaps the best idea of the nature and pedigree of these living particles will be gained by a study of Haeckel's kingdom of Protista, to which, if true organisms they really be, these granular bodies must belong.*

How then, it might be inquired, would specific micrococci operate as the proximate cause of the equally specific morbid process of general tuberculosis? The question is thus stated, because, although a probable causative action of these organisms has been surmised, in a general way, the *rôle* played by them in the pathogeny of tubercle, has never, as far as I can learn, been thus theoretically considered; while, indeed, most pathologists have hitherto done no more than discuss the mere fact of the existence of those organisms, and mainly as incidents among the products of decay.† I therefore venture to

* Excellent facility for this study is now afforded to the English reader in Professor E. Ray Lankester's recently published translation of Professor Haeckel's *History of Creation*. 1876.

† Dr. C. J. B. Williams, *On Pulmonary Consumption*, p. 98.

think they will probably be found to operate as the exciting, efficient, or, better termed, proximate, cause—the *materies morbi*, of tubercle, somewhat in the following manner :—

The protoplasm out of which an epithelial cell forms on the wall of an alveolus is chemically composed of a protein substance holding salts of lime and other mineral ingredients in solution, in combination with phosphorus. The various elements are doubtless bound together in some form or compound resembling glycerophosphoryle; but the facts of ultimate analyses are ascertained beyond any doubt. As it is a known action of microzymes, in their mode of life as fungoid organisms, to absorb nitrogen compounds, their proper nutriment, from any albuminoid matter in a changing or an unformed state,* such as protoplasm, that they may come in contact with—to feed upon it, and in their way multiply, like other fungal parasites—so will these microzymes naturally

* Micrococci develope wherever there is moisture and nitrogen available for assimilation.—Professor Burdon-Sanderson, *Rep. Priv. Council*, 1874. See also a paper on *The Phenomena of Fermentation*, read before the Pharmaceutical Society of Victoria, by Mr. W. Johnson.

operate destructively on the protoplasm of the nascent epithelial cell, withdraw nitrogen, and with that element inhering kinetic force, liberate pent up potential energy,* and leave the other chemical elements remaining in the impoverished protoplasm, to obey passively their physical statics, and separate, by a spontaneous lysis, into an insoluble compound of lime salts with fatty matter, setting free the constituent glycerine, and retaining calcium phosphate in the mechanical mixture. This is the actually known chemical composition of the aggregation of blighted epithelial cells impacted by a process of gradual accumulation, in mass in a lung air vesicle, and termed, according to its mechanical figure as presented to the naked eye, a miliary nodule or tubercle.

In this mass of epithelial debris the minute bodies of microzymes are set embalmed, or

* Energy has as much claim to be regarded as an objective reality as matter itself."—*The Unseen Universe*, p. 81. The modern physicist's dogma of potential energy and kinetic force, differs in nothing, save in terms, from Hobbes's doctrine of Power and Act, in his exposition of *Cause and Effect.*

buried as it were in the ruins they produced. To rightly understand the entire process of tuberculosis, it is necessary thus to consider, not only the operation going on in a single air vesicle, but even in a solitary epithelial scale; for of an infinite number of such single actions the whole process is an aggregate.

It was obviously impossible to ascribe to micrococci an exact chemical composition, or to assert absolutely that their constitution is, though not entirely yet very largely, composed of nitrogen constituents, while they had never been separately collected or analysed; their composition was, therefore, only theoretically inferable by analogy; although even that may not be complete, inasmuch as many fungi largely consume the phosphorus that forms a constituent of protoplasm. In separating bacteria to test their power of septic infection, Hiller has not, as far as I am aware, tested their chemical composition by analysis. The recent experiments of that pathologist tend to prove that if micrococci parasites be not of themselves capable of decomposing albumen by assimilation, they are probably the carriers

of the septic poison, which they "perhaps" produce or reproduce.*

If these minute bodies be really true disease germs, and specific organisms,† their history is so far only traceable by induction. If all disease germs, or contagia, be not distinct organisms, but are, what Dr. Lionel Beale contends, merely detached masses of bioplasm in an over-active state, then their chemical nature would be that of the stock bioplasm of which they primarily formed a part.

The same chemical nature enables us to explain subsequent changes that occur, after this necrosis of the epithelial protoplasmic

* This septic virus Hiller thinks, after Liebig, is a dead animal ferment, rather than a living organism, but the proofs he offers are not stronger than those on the other side; while the strongest argument is the fact that moners do live by decomposing protoplasm in the ordinary act of assimilation.—See *Ed. Med. Jour.*, Jan. 1876, p. 653.

† Although they may not be properly termed organisms in the sense of their possessing separate organs, they yet are plastid particles, or moners, of a distinct living individuality. That is to say, that being of the protista they are neither of vegetal nor animal nature or origin, nor dependent upon their habitat for their characteristics. In other words, they are specific organisms, developing wherever they obtain their appropriate nutriment.

mass, under fatty degeneration, and further retrograde metamorphosis occurring during chemical decompositions prior to absorption of tubercle, its calcification or cretification, or softening, in the various stages or forms of tubercular phthisis; and it also fully accounts for the peculiar chemical characteristic qualities of tubercular sputa.

The presence of glycerine in the sputum explains the sweetish taste that clinically augurs so ill. The fact also affords an adequate reason why, although sweet, phthisical sputa yield no evidence to tests for sugar; the tests for sugar and glycerine not being the same.*

The action thus set up by micrococci would constitute tuberculosis a true mycosis. This febrile state, defined by Dr. Burdon-Sanderson, consists in an infiltration into any part of micrococci, with consecutive morbid actions, in the form of local acute or subacute inflam-

* Traces of glycerine have been found by Hertz, as a product of the decomposition of albuminoid matter in the sputum in gangrene of the lungs, but I do not know that it has been detected in the sputa of tuberculosis.—*Ziemssen's Cyc.*, vol. v. p. 417.

mations, produced by the irritation of dead epithelial waste matter acting as a foreign body, resulting condensation of lymphatic or adenoid into fibroid tissue, and constitutional sympathy or fever.

If the explanation here offered be found true, it will fully account for the febrile symptoms occurring on every fresh swarming or multiple of the parasites; also, for the consecutive anatomical lesions in the trabeculæ, inter-alveolar growths in the cytogenic or adenoid tissue, hyperplasia, development of perivascular cords, vascular infarctions, obliteration of the capillary network, and the formation of minute aneurisms. The amount of protoplasm being always greater in early life than at later ages, would account for the greater proneness of youth to tubercle. In short, this would be found the initiative, and therefore the efficient, cause of tubercle; which, in its turn, is by many admitted to be the irritant setting up the secondary changes that constitute true phthisis. I say *true* phthisis in contradistinction to the several forms of chronic wasting disease commonly called phthisis, from their

clinical resemblance to the real affection, but which are to be both etiologically and pathologically distinguished; such as is the form often complicating diabetes, wherein the tubercle-like nodules are, according to the observations of Dr. Addison, Dr. Wilks, and Dr. Pavy, and more recently of Dr. Hilton Fagge and Dr. Dickinson, produced by a form of caseating pneumonia, and not by tuberculosis, which they merely simulate.

Eventually the above theory might become directly clinically instructive by pointing towards a rational method of preventing phthisis, and of making it in turn become a "pathological rarity." Or, if not that, of attacking it before permanent tissue change or decay occurred, to secure its arrest, or cure, by agents, such as quinine, experimentally known to be destructive—germicidal—of the organisms occasioning this epithelial blight.* For, while it is but an idle

* The term "*blight*," here applied to tubercle, is used in a different way from that employed by Dr. William Addison, who wrote of pulmonary tubercle as "blighted granulations." The cause of epithelial blight was an organism then unknown to natural science. That physician

truism to affirm that the healing art never can restore lost normal lung structure; so does it seem premature to assert the improbability of ever finding means of killing parasitic particles in living tissue, without at the same time destroying its own integrity; and this simply because the individual spec of bioplasm forming a *moneron* may have less inherent vital resistance than the formed tissue of the higher organisms.† Preparations of mercury, iodine, arsenic, and other medicines of the class, so well known for their power of destroying parasitic life upon the exterior bodily surfaces, may operate in precisely the same manner on analogous organisms existing upon the interior surfaces. Thus indeed may be explained the effect of mercury in syphilis, and of the famed Tanjore pill, formed of arsenic, in leprosy.

This blight theory accords with the "guesses" of others. Thus, in one of our best text-books

thought that, not the mere presence of tubercles was consumption; but the destructive changes set up by them in the contiguous lung stroma.—Addison, *On Healthy and Diseased Structure*, p. 77.

† *Practitioner*, Jan. 1876, p. 10.

of pathology, the authors, alluding to tuberculosis, state that "It is not proved that "some miasm or atmospheric influence is "not concerned in its production," but add nothing of the probable form in which it exists.* Has it not life, to act like Lister's germs in open wounds, that take plastic power from granulating protoplasm, and leave *debris*

* The third edition of Dr. T. H. Green's *Introduction to Pathology and Morbid Anatomy* contains the following corroborative new sentence, added, at page 228, to the article on *Acute Tuberculosis:* "It is also possible that the infect- "ive properties of an inflammatory product may be deter- "mined by atmospheric influence, *or by the presence of* "*minute organisms.*" The italics are mine, to denote the point of reference. So, likewise, Surgeon Alcock, of the Army Medical Department, in an essay *On the Nature and Variation of Destructive Lung Diseases included under the head of Pulmonary Consumption*, &c., speaks of "devitalized leucocytes" forming "a nidus of dead "material," upon which "impure gasses in the vicinity "effect such changes as to render it a focus of inoculation "to the adenoid tissue of the part." Also, in the manual of Jones, Sieveking, and Payne, already cited, it is stated that "In vomicæ there have often been found the minute "organisms (micrococci and bacteria) which accompany "putrefaction" (p. 507.) But none of those allusions to the action of these bodies ascribe to them the special function claimed for them by the hypothesis here enounced. The idea of Surgeon Alcock is the nearest approach to it that I have met with, although probably, all may be

pus particles? In the leading views now entertained of tuberculosis, viz.: as blastema effused and organised into miliary tubercle, free cell formation within a vein, tubercle formed by proliferation from elements of the tissues, in fibroid growth of adenoid tissue, from white cells of blood transmitted through the walls of vessels, or of the germination of endothelial cells around lymphatic pseudo-stomata, no hint appears about the action of a miasm, or of any kind of living organism as a destructive parasitic agent.

The idea of micrococci being in any way associated with the process of tuberculosis is a

included in Kleb's theory of "epithelial infection." In his treatise *On Stethometry*, 1876, Dr. Arthur Ransome states that he found in the watery vapour from the breath, in a case of phthisis with albuminuria, "abundant specimens of a small round-celled conferva;" which he, however, does not think sufficient to afford any proof of the germ theory of disease. In a very full account of the various kinds of fungoid particles found in the sputa, given by Prof. Hertz, in *Ziemssen's Cyc.*, vol. v. p. 417, and again at p. 469 of the same volume, on the vegetable parasites of the lungs, nothing appears about the presence of micrococci in causative relation to morbid action herein described, for their existence is thought only to indicate the results of putrefaction.

recent one; and the explanation of their mode of operation is, at least, as far as I am aware, now for the first time in the history of pathology attempted, with what degree of success remains to be seen.

This view would derive little from analogy, even if Lostorfer's theory of the cause of syphilis had been verified. As yet only the blood in syphilis has been explored.* But, where the semen has been the contaminating agent, as it alone can be in latent syphilis, a spermatozoon must have been the vehicle conveying the specific contagion, and there in it might have lain the infecting parasite, very probably in the form of microzyme. This proposition has a perfect analogue in the discovery, by Pasteur, of *pebrine* in the diseased ova of silkworms, into which the parasite must have passed along with the spermspore.

In a similar manner may inherited syphilis be readily accounted for, whether derived from male or female parent: spermatozoon or ovule; and thus show why it is that germs

* Prof. Bäumler, *Ziemssen's Cyc.*, vol. iii. p. 54.

of tubercle, like germs of syphilis, persistently inhere in direct lines of descent.*

Whether the micrococcus of syphilis be ever capable of devolution into that of tubercle, as is often conjectured about the clinical histories of both diseases, the twin ills of one heir-loom, may become a question for investigation in the future study of its morphology. In tubercle as in syphilis, it is the endothelial and epithelial systems that are peculiarly invaded. Racial peculiarities may suggest a reason. Among a people peculiarly free from syphilitic and tubercular diseases, the habits and rites that guard against the one malady, may equally ward off the remoter sequence.†

* In declaring his belief that hereditary predisposition has been much over-rated as a cause of phthisis, Mr. Huth adds that all causes which tend to a diminution of vital power are causes of phthisis, which if true, as it certainly is not, would make the disease non-specific. But Mr. Huth admits (of phthisis, &c.), that, "so far from their real origin "being even tolerably clear, they are involved in great "obscurity; and that we should know what other causes "are generally assigned to these scourges of humanity, "before we attempt to judge that alleged by the "Parasyngeneiasts."—*The Marriage of Near Kin*, 1875.

† See *Diseases of Modern Life*, by Dr. Richardson, 1876, p. 23; and *Phthisis and Climate*, 1870, p. 113.

In every community where syphilis greatly prevails there is also much phthisis; but I am not aware that nations noted for an immunity from the latter, are also markedly free from the former, although it is probable that upon inquiry the two diseases will be found invariably associated; but whether they are in any way genetically connected there is no positive knowledge to warrant scarce even the bare surmise.

The growth of tubercle has before now been attributed to parasitic action,* but in a way wholly different from that above described.

The view confirms the theory advanced by Dr. William Budd, that allied the affection causatively to the acute specific fevers, and would, therefore, prove it to be, like its congeners, etiologically independent of the influence of climate.

That tubercle really springs in epithelial cells on the alveolar septæ can no longer be doubted. In the latest researches of Dr. Klein, that observer has "followed their develop-

* Dr. Baron thought tubercle was due to the action of hydatids.

"ment from the epithelial cells of the alveoli "with all possible certainty;"* while Professor Küss (of Strasburg), states that "*Tubercle* is *hypertrophy* followed by a sort of *mummified deposit*, formed by the epithelium, a definition of tubercle that agrees with the remark of Frey about "the peculiar withering of cells in tuberculisation" (*Hist.* p. 95), and likewise with the later researches of Bastian, proving the origin of meningial tubercle to be from decayed endothelial cells of the perivascular sheaths—the adenoid tissue of His—of the cerebral arteries.† Those authors, however, offer

* See *Rep. Priv. Coun.* No. iii. p. 42, 1874. It is proper here to state that a different view is taken by Prof. Rindfleisch, who, in combating the view that phthisis is primarily only a catarrhal inflammation beginning in the smaller bronchi, maintains that tubercles are "not infundibula filled with the products of inflammation, but tubercular infiltrations of the connective-tissue angles at the points where the bronchioles become continuous with the acini."

† Dr. Wilson Fox alluded, in his opening address at the debate on tubercle at the Pathological Society, to the decayed epithelium in tubercle, calling it "perished epithelium." I refer to the opinion of Dr. Bastian, although Professor His modified his account of the peri-vascular sheaths.

no other explanation of the mummifying process; any more than do Klebs, or Green, at least as far as I have been able to learn, afford an explanation of the manner in which the organisms they speak of operate. A histochemical consideration can alone explain the relationship of these organisms to the deposits of mummified or blighted epithelium, forming grey granulations or miliary tubercles, and the further relation of these to the associated phthisical state. It is warmly debated by pathologists, whether the local inflammation or the tubercles come first; but, by the explanation now offered, their occurrence would be simultaneous.

If miliary tuberculosis "has clinically the "character of an 'infective' or so-called "zymotic disease," wherein resides the propagating agent? If the fever be like other zymotics, depending on living organisms as the exciting cause, it must obey in that particular the law of the class it belongs to. The enlargement from interstitial growth of the liver and spleen, so common in specific fevers and in tuberculosis, show by analogy that they are

probably allied, and, therefore, alike caused by microzymic contagium. It may even yet be found that in this pathology is contained the key to the explanation of the fact of tubercular disease supplanting intermittent fevers in districts where paludal malaria are removed by drainage or cultivation; and this appears to me a better explanation than that which Hirsch has offered, of simultaneous changes in the habits of the people. The introduction of trades and factories into a wilderness means the crowding with population, and consequent increased facilities for propagating the germs of a specific contagion.

In the early days of this colony, tradition says there was much fever of intermittent type. Now, however, there is none of it; but instead much phthisis. The one malady *may* have replaced the other, though for the belief there are no clear data extant.

By the advocates of the contagiousness of tubercle, the germs are usually said to be spread about by the drying up of the sputa, the resulting impalpable dust flying about in the air around the sick person; but it has

never before been explained in what these infecting germs or particles consisted.

The new hypothesis further accords with the now almost universally held theory, first enounced by Buhl, and afterwards elaborated by Weber and Waldenburg, that explains the origin of the process of tuberculisation to be the absorption of caseous matter out of deposits in the lungs or other parts of the body, the relics of former inflammations, acting as infecting centres. It is quite admitted, as was lately explained,* that as long as the capsule of the cheesy mass, be it large or small, remains intact, there can be no removal of particles to act as infecting matter; but that the moment after a breach of continuity occurs in the limitary membrane, absorption and infection begin. Beyond the mere statement of the sequence of events, I am not aware of any attempt to trace the mode of action of the infecting agent, or in any way to explain the process, and the following conjecture may suggest or direct further re-

* Dr. Tuckwell, *Lancet*, Dec. 11, 1875.

search.* While the caseous centre remains encapsuled the external air is excluded; but a breach in it, caused by ulcerative absorption, allows access by the germs of micrococci, the invariably present active agents of putrefaction, for the disintegration and removal of the dead mass, imbedded as a foreign body within the tissues of the living organism. These germs, by developing and multiplying, naturally migrate through the afferent channels of the lymphatics to the lymphatic glands, organs that are best described as "originally plexus of lymphatic capillaries, ramified, anastomosed, and rolled up into a ball," to economise space. There the parasites will operate upon the epithelial lining, shown by v. Recklinghausen in the lacunar lymph spaces of Frey, exactly as they do on that of the air sacs, the resulting

* Some time ago a caseous mass was sent to me by Mr. Graham Mitchell, V.S., for examination. It was the size of a walnut, with the capsule intact; but as I did not see the lungs of the cow from which it had been removed, *post mortem*, I had no opportunity of observing whether or not there were any co-existing miliary granulations. I mention this circumstance, because, to town dairy milk has been attributed much of the atrophy and tubercular disease so prevalent in this city.

morbid products being of precisely the same nature, all the difference of appearance arising alone from the different form of the matrix in which the process goes on, being soft and diffluent in the medullary stroma of the lymphatic gland, but firmly bound down in the unyielding texture of the alveolar walls; and hence explaining how miliary tubercle and strumous gland matter are identical pathological products. If, on the other hand, the micrococci be taken up by the venous radicals they will equally readily be conveyed thence through the capillaries of the pulmonary artery, and thus finally reach the alveolar walls of the air vesicles, where they will operate again upon the freshly exuded protoplasm designed for the epithelial renewals, as already explained. By their nature these plastid particles of hyaline will possess the power of amœboid movement, like leucocytes, as shown by Conheim, and will readily pass through the capillary walls. Here, then, is quite a clear and consistent, as it is a simple, account of an infecting process that has been abundantly demonstrated as far as facts are

required, although hitherto without the accompaniment of any explanatory rationale. But it yet remains to be shown that the secondary lesion induced by absorption of particles from a caseous deposit is identical with the idiopathic form, or quite a different one, more resembling that produced by inoculation. If the latter, it would be the basis of a clearly defined pathological distinction between two phthisical states clinically alike.

The form of phthisis following initial hæmoptysis, explained by Prof. Niemeyer, and afterwards clinically described by Prof. Baümler, can be similarly accounted for by inferring the action of infecting organisms on the clot detained in the affected bronchiole.

By applying the same line of argument, or ratiocination, to explain the production of miliary granules by inoculation of either tubercular matter or other non-specific irritants, as has been tried by Villemin, Klebs, Fox, and other experimentalists, the process will, probably, be equally fully elucidated. At the present time some such suggestion as is here submitted for the consideration

of pathologists might be found of value, because, in the very recent series of crucial experiments performed by Metzquer the negative results lose much of their intrinsic value, through wanting a guiding clue to their interpretation.

It may be further objected, that nothing here would account for the different results of absorption from various infecting foci, in one case causing pyæmia, as recently explained by Mr. Savory, while in another tuberculosis occurs.* But, if we admit the probability of some microzymes having specific characters, as was claimed for them by Dr. Burdon-Sanderson, in his original account in the 12*th Privy Council Report*, 1870, page 255, the difficulty is at once overcome. There cannot be a doubt that, if contagia do really exist in the form of minute living organisms, their specificity must be as exact and different as are the fevers they produce.†

* It is now maintained by Dr. Braidwood that the state produced by inoculating animals with various irritants, is not true pyæma, or suppurative fever. See *Lectures on Surgery*, by Prof. Spence, 1875, p. 32.

† And here I shall add a single word on the theory

True or not, the hypothesis is at least more suggestive of inquiry than is pronouncing the cause to be "a mysterious something," as was last year admitted in the leading columns of the London *Medical Times and Gazette*; or most contentedly saying with Dr. Green, that the morbid processes of phthisis "owe their origin to *some kind of injurious irritation*;" this irritant being the "common unknown cause"

of the specificity of germs as excitors of specific febrile action. It was denied by the opponents of the germ theory that any distinct form of germ could be differentiated, and that that failure was an irrefragable argument against the truth of the doctrine. But they forgot that the difference had at that time to be shown by a physiological process, and not by a mere physical aspect. What would a germ grow up to? was the query. It appeared to be requiring too much of histology to call upon it to distinguish the physical marks of various micrococci, at least until they became developed into colonies, as bacteria or zooglea, when probably their toxic powers cease, agreeably to the general law of animal poisons; shown in their greater virulence shortly after death, than when decomposition has made progress, under the growth of the agents of putrefaction. But the argument is now finally met by the demonstration of specific forms of living contagia, as definite, observes Mr. Simon, in reference to Dr. Klein's remarkable discoveries, "as the forms of the higher plants or animals;" and by processes "as exact as a laboratory experiment."

of tubercle, referred to by Billroth, showing that pathologists had not yet defined Buhl's infecting agent. Nor have the very latest researches on the etiology of phthisis apparently advanced beyond the general term, for in Dr. Pollock's lectures, now being published, *adenoid* is described as *growth under irritation*, the nature of the *irritant* not being mentioned.* Equally indefinitely does Rindfleisch allude to the giant cells of tubercle as "mysterious objects;" and also "assume that in the primary inflammatory focus a special tubercular poison is elaborated," in the catarrhal secretions of a scrofulous person, but without further speculating upon its probable nature or genesis. So special a poison must surely be a noticeable entity.

Of the primary nidus of the contagium particles, various views may be held. They may be developed in the morbidly acid alvine secretions, so frequent in tuberculosis, and a condition always favourable for the growth, or, as some think, origin *de novo* of parasitic

* *Lancet*, March 18, 1876.

organisms. Thus would be associated many of the premonitory intestinal states prodromal of an attack of tuberculosis.* The organisms may be the micrococci of Cohn; the microzymes of Béchamp; or they may be possibly associated with the common septic ferment, as suggested by Simon, and therefore be of non-specific nature; although there is no apparent reason why the microzymes of tubercle should not be as specific as those of yeast or of syphilis.

But again, there is furthermore very strong analogy in favour of the accuracy of the view in recently discovered *psorospermia* within the columnar epithelium of the small intestines, where parasitic organisms consume protoplasm, and leave *debris* keratin of wasted or blighted epithelial cells. In Frey's *Histology*, page 93, several illustrations are given of these organisms that were thus found in the epithelial cells of the small intes-

* Yeast is always acid. "The diffusable products formed "by stomachic, intestinal, or artificial digestion, show "themselves to be eminently suited to nourish the cell of "the *Saccharomyces*."—P. Schützenberger *on Fermentation*, 1876, p. 85.

tines of rabbits.* It is not impossible, nor improbable, that a migration of such fungal organisms goes on through the lacteals† from the alvine track to the remoter seats of tubercular action, verifying the opinion, long held by many, of the origin of tubercular disease being not where deposited: not a local but a general disease; a view that would afford a perfectr ationale of the doctrine enounced by Dr. Wilson Philip, and Prof. Bennett, so well known to pathologists. So, likewise, would thus be explained the "vulnerability" of Niemeyer, in those hereditarily predisposed, who are only

* At page 190 of the eighth ed. of *Carpenter's Physiology*, 1876, numerous references are made to the various authors who have described these psorosperms, none of whom have, however, attributed to them the important action now proposed. The destruction of epithelium thus produced resembles, but is not identical with, the process of vacuolation resulting in the removal of the protoplasm from the cells in cancer, as explained by Dr. Creighton, in his *Anatomical Research towards the Ætiology of Cancer*, in *Priv. Council Rep.*, p. 95, 1874.

† The possibility of such a migration of solid particles of colloidal matter is now no longer doubtful, but made certain by the modern discovery of the openings of channels into the lacteal capillaries through the goblet cells of the intestinal villi.

in greater risk through more intimate exposure to the specific agent; while it might even be found to explain why the phthisical are in danger of becoming tubercular, according to the inflammatory theory of that great teacher; for they always are liable to re-infection. In fine, the theory comprehends predisposition, in all debilitating conditions of life, to the inroads of a parasite that, like its congeners, is ever ready to sieze bodies prone to decay. In this particular it would differ from other specific contagia having a mycelial growth, for the latter appear equally ready to attack the strong or the weak. The existence of the parasites in single monads, and never in chains or zooglea, may have added to the difficulty of determining their true nature.

Before a hypothesis can attain the completeness of tenable theory, it must enable us to interpret, or reconcile with it, all known phenomena of the science of the particular subject to which we apply it. Trying the present conjecture by this test, it may now be further extended to expound the rationale of the facts experimentally observed in the artificial induc-

tion of tubercular fever by feeding animals on milk drawn from dairy cows labouring under the naturally induced disease. By making various animals, guinea pigs, rabbits, or calves, injest this diseased milk, Gerlach, Klebs, and many others, have frequently produced well-marked tuberculosis; so often, indeed, that this milk has lately become suspected of being one of the commonest modes of propagating tubercular disease, especially amongst children.* This opinion is held by Mr. George Fleming, of whose writings on comparative pathology, none is more suggestive than the chapter on *Tuberculosis in Cattle.*† In describing the physical appearances and chemical characters of this morbid milk, Mr. Fleming remarks that in the first stage of disease it is more watery, bluish-tinted, and "*contains a larger proportion of alkaline*

* It was disappointing not to find any information upon this point in Mr. Smee's work. That author merely observes that,—"The milk of phthisis is said to be greatly "altered ; but I regret that I have not been able to obtain "specimens of milk from this disease for examination."—*Milk in Health and Disease*, by A. Hutchison Smee, 1875.

† *Manual of Veterinary Science and Police*, vol. ii. p. 368.

"*salts; but it is less rich in nitrogenous matters*, "and fat and sugar, than in health." In the second stage of the disease "*the milk is markedly* "*diminished in quantity* and quality, as already "mentioned, being blue-coloured and watery, and "*poor in nitrogenous matters*, butter and sugar; "but *rich in mineral constituents*."

After some remarks about the food-value of the flesh, its pale, watery, bloodless state, as was elaborately shown in the experiments of Dr. William Marcet (though Sir James Clark said it was preferred by tender epicures), Mr. Fleming proceeds to discuss the food-value of milk, in which he particularly cites the experiments of Klebs to test its disease-producing action. The results led that observer to conclude that the use of this milk sets up tuberculosis, by first exciting intestinal catarrh, and next mesenteric tubercle; attacks then the liver and spleen, and finally the thoracic organs. "He (Klebs) asserts that *the tuberculous virus* "exists in the milk of phthisical cows, whether "they are slightly or seriously affected, and "that it is *chiefly in the serum;* as when the "*milk has been* so filtered as to deprive it of

"its solid particles, the fluid portion appeared "to be as active as the unfiltered. Its virulency "is not destroyed by ordinary cooking."

It may now be asked, in what form does the virus exist in the serum? If as micrococci, they would not be filtered out of it by any common filtering process sufficient to stop the passage of ordinary milk globules, for those parasitic creatures are less than the 20,000th of an inch in diameter, minor milk globules being perfect giants beside them. Hence the serum would still retain virus and be as active as the milk itself, just as in Chauveau's experiments with vaccine lymph, diluting it and filtering it to get rid of the normal serum leucocytes, but requiring dialysis to exclude the virulent microzymes, a process which does not appear to have yet been tried in the case of the milk serum in phthisis.

The explanation of these varied facts would, therefore, appear to be somewhat as follows:

The secretion of milk in the acini of the enlarged sebaceous* mammary gland goes

* It has often occurred to me that in the colliquative sweats of phthisis the fluid ran from the sebaceous

on through a continuous moulting of the epithelial cells,* every cell being but a vehicle for carrying away a globule or particle of milk.† If micrococci were present, they would (as before explained), attack the protoplasm of the nascent milk globule, appropriate its nitrogen, and, destroying the vital integrity of the particle, leave the remain-

follicles rather than from the sudoriperous glands, because of the dryness of the palms of the hands and soles of the feet, where there are no sebaceous follicles or glands, and from the damp or even *wet* state of the hair in both man and other animals affected with the disease; and the opinion is so far corroborated by an observation made by Küss, that the epithelial cells of the sebaceous follicles often contain serum in lieu of fat. If my conjecture be correct, it would explain the reason for the remark of Ruelhe, that "whether the perspiration in phthisis has any special qualities is unknown."

* A full discussion of this point is contained in the *Priv. Coun. Rep.*, 1874, p. 189, by Dr. Creighton, who quotes M. M. Cornil and Ranvier, with many more authorities.

† It should be borne in mind that the epithelium of the air vesicle of the lung takes no part in the function of secretion, so that the effect of the destructive action of a parasite on its protoplasm would differ from the effect of similar action on the protoplasm of secretion epithelium, the debris of the cells being washed away in one case, and in the other retained to form tubercle.

ing ingredients to form a watery fluid, poor in nitrogen, and apparently abounding in calcareous or earthy matter. This fluid would not only be innutritious, because the potential energy primarily imparted by the nutrient secreting gland for transmitting to the recipient would be removed therefrom on being discharged as kinetic force to bestow vital activity on the parasite; but it would be further actually poisonous when so charged with living contagium of specific disease. This diversion of potential energy from host to parasite explains the extreme sense of debility always felt as the earliest premonitory symptom of tuberculous fever. The abnormal diversion of potential energy is doubtless the true cause of that loss of nervous influence which lowers the temperature, as tested by the thermometer, in the pre-tubercular or preliminary febrile stage of tuberculosis; or rather, in other words, when the fever of tubercular mycosis is still in the incubative period, the state corresponding to the cold stage of all fevers, exists. The aspect of the milk corroborates this view; for if such a fluid be

allowed to stand in a conical glass, it will often deposit a precipitate of solid calcareous matter, giving the appearance of an excess of earthy ingredients. But this is a delusive appearance, since the true reading of the fact is that the integrity of the casein, as the nitrogenous solvent of the phosphates of lime, magnesia, and iron, in the normal milk, is broken up by the withdrawal of the nitrogen, the mineral ingredients, now no longer held in chemical suspension, fall physically as mere inert matter in the morbid fluid. This dead stuff is then in the form of *phosphates*, having been thereto probably reduced from some higher or really vitalized bio-chemical condition, or, as Dr. Marcet would perhaps explain, by their conversion from the colloid into the crystalloid state. It has been doubted by many if there is really any class of salts corresponding to that constitution existing in nature, or out of the chemist's laboratory; and that the belief of their existing in milk in any other form than that of phosphates is perfectly gratuitous. But, the opinion offered of their existence in forms other

than phosphates has for support the special authority of Fownes,* who observes :—"We "find, besides, associated with this casein, a "large quantity of earthy phosphates held in "solution in a very extraordinary manner, in a "neutral, or even slightly alkaline menstruum." And further on he adds :—"It is stated by "Mulder and others, who have made casein "the subject of their inquiries, that this body, "separated by precipitation from milk, contains "no unoxidized phosphorus ;—a substance "*present in both fibrin and albumen.* Now, "it is very certain that milk alone is fully "competent to the nourishment of a young "animal ; that is to say, to the production of "every part of its body, including those which "contain phosphorus in the state referred to. "Either, therefore, the animal system must have "the power of deoxidizing phosphoric acid— "a thing little probable—or some yet unknown "source of phosphorus exists in milk which "has escaped observation." As the lower oxides of phosphorus were not much thought

* *Chemistry, as Exemplifying the Wisdom and Beneficence of God.* 1844, pp. 144, 174.

of in Fownes' time, their existence might, had they been then as well known as they are now, have supplied his desideratum.

The later discussions about the value of different foods that would alter the ideas about them, which were formerly derived from Liebig's views, and tend to prove that a source of mechanical force exists in non-nitrogenous substances, do not affect the principal conclusions drawn from the comprehensively nutrient quality of milk.*

In speaking of the causes of tuberculisation, it is not enough to allude to them as mere forms of impaired nutrition, for pathologists ought to be ready to explain how defects of nutrition lead to definite if not specific disease; neither is it enough to affirm generally that when vital force fails chemical forces come into play; for that generalisation is equally true of all forms of living decay, or necrobiosis. What is required is a descriptive account of the mode in which the action of decay proceeds. Mere starvation will not

* Hermann, op. cit. p. 224.

induce tubercle. Neither would repletion alone ward tubercle off. The use of alcohol often will prevent tubercle, because alcohol, like quinine, kills micrococci. This indeed might be found to be the true rationale of the action of antiseptic inhalations in phthisis; and it would also explain how the same antiseptic property of quinine, as shown by Binz, becomes directly curative of phthisis, by arresting the parasitic cause of the destruction of epithelium.* There can be little doubt that the mode of action of bitter tonics and

* By acting on this theory of the effect of quinine, I have lately seen marked results from its use in malignant scarlatina. During the present severe epidemic of that fever, fourteen well-marked cases of the most malignant form have come under my notice. Of these eight were fatal, with six recoveries. In none of the fatal cases was quinine given; but in all the six cases, equally severe, that got well, the patients all being mere children, the medicine was given in doses of from five to eight grains every hour, day and night, for several days, one boy of ten years old taking four drachms within three days. Whatever the explanation, it is certain that, as shown by Hallier and Riess, the blood in scarlatina swarms with micrococci; that the indicated remedy, in those cases at least, did its work; that the same agent is known to be one of the most potent over phthisis; and that, therefore, the clinical example may strengthen the pathological analogy.

condiments is entirely through the prevention of the evolution of intestinal psorosperms. Dr. C. J. B. Williams suggests that the beneficial effect of sulphuric acid in phthisis may be partly wrought in this manner; and the limited therapeutic principle may, probably, be found equally applicable to the more extended pathological theory.

And if, therefore, it were now asked how a remedial operation could result from the use of substances of definite chemical constitution under the epithelial blight theory, it would be enough to reply that such substances are not drugs in the ordinary sense of the term, but peculiar forms of food, easily assimilable, and supplying the elements of nutrition that are rapidly consumed to maintain the morbid process. The integrity of the body has to be conserved against the myriads of organisms preying to its destruction. Drugs may be found to destroy the parasitic cause of the disease, as drugs have been found effective in analogous cases: in the power of mercury over the parasite of syphilis, of arsenic over that of leprosy, empirically discovered before

being scientifically explained; but in every form of tubercular decay a physiologically indicated form of nutriment must be employed to repair, as far as is compatible with lost or permanently altered tissue, the effects produced by the epithelium invading parasite.

THE END

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By the same Author

ON

PHTHISIS

AND THE

SUPPOSED INFLUENCE OF CLIMATE

BEING AN

Analysis of Statistics of Consumption in this part of Australia

WITH REMARKS ON THE CAUSES OF

THE INCREASE OF THAT DISEASE IN MELBOURNE